SUSTAINABLE INFLUENZA VACCINE PRODUCTION CAPACITY

Cost Considerations: Ensuring the Best Returns on Investment while Ensuring Sustainability and Diversification

Barry R. Bloom
Harvard School of Public Health

Outline

- Economic Costs of Influenza and SARS
- Economic Risks and Benefits in Vaccines
- Innovative Financing for Vaccines

INFLUENZA PANDEMICS IN 20TH CENTURY

Credit: US National Museum of Health and Medicine

1918: "Spanish Flu" A(H1N1)

40-100 million deaths

1957: "Asian Flu" A(H2N2)

1-4 million deaths

1968: "Hong Kong Flu" A(H3N2)

1-4 million deaths

How Serious is an Epidemic and How Quickly will it Spread?

- Larger world population (3 x that in 1918) and greater population density
- Increase in international travelers (312 million to US, 2004) and speed of travel since 1918
- Experience with SARS: 31 countries affected between 2/21–6/10, 2003
- Between May 4 and July 31, 2009, 168 countries reported at least one laboratory confirmed case of pandemic (H1N1) 09

ESTIMATED ECONOMIC COSTS OF SARS

	Reduct Ann Growth	Reduct in Ann GDP
• PRC	0.6%	$7.2 billion*, $3.5 billion**
• Hong Kong	1.8-4.0%	$3.0-6.6
• Rep of Korea	0.2-0.5%	$1.3-3.0
• Taiwan	0.9-1.9%	$2.5-5.3
• REGION	0.4-1.0%	$16-30 billion*
• Canada		$30m/day $9.5 billion

**NYTimes*

ADB: SARS Economic Impacts and Implications (Fan, E.X.) May 2001

*-**Keogh-Brown, et al. Health Policy. 2008*

Projections of a Flu Pandemic in the US

- Expect up to 200 million people infected
- 38-91 million people clinically ill
- 314-733,000 requiring hospitalization
- 89,000-207,000 deaths
- Health care workers at highest risk

- Mild Epidemic would cost 1% GDP
- Severe Epidemic would cost 5% GDP/ $500 billion

DHHS National Pandemic Influenza Preparedness Plan, 8/2004

CBO Report A Potential Pandemic Influenza Epid 12-08-05

How Do We Know How Serious and Epidemic Is? Case-Fatality Ratio: Range of Estimates

- Mexico May 4
  - 509 confirmed
  - 19 deaths (4%)
- US May 4
  - 268+786 confirmed + probable
  - 1 death (0.1%)
- Censoring bias (missing deaths)
- Detection of mild cases (missing cases)

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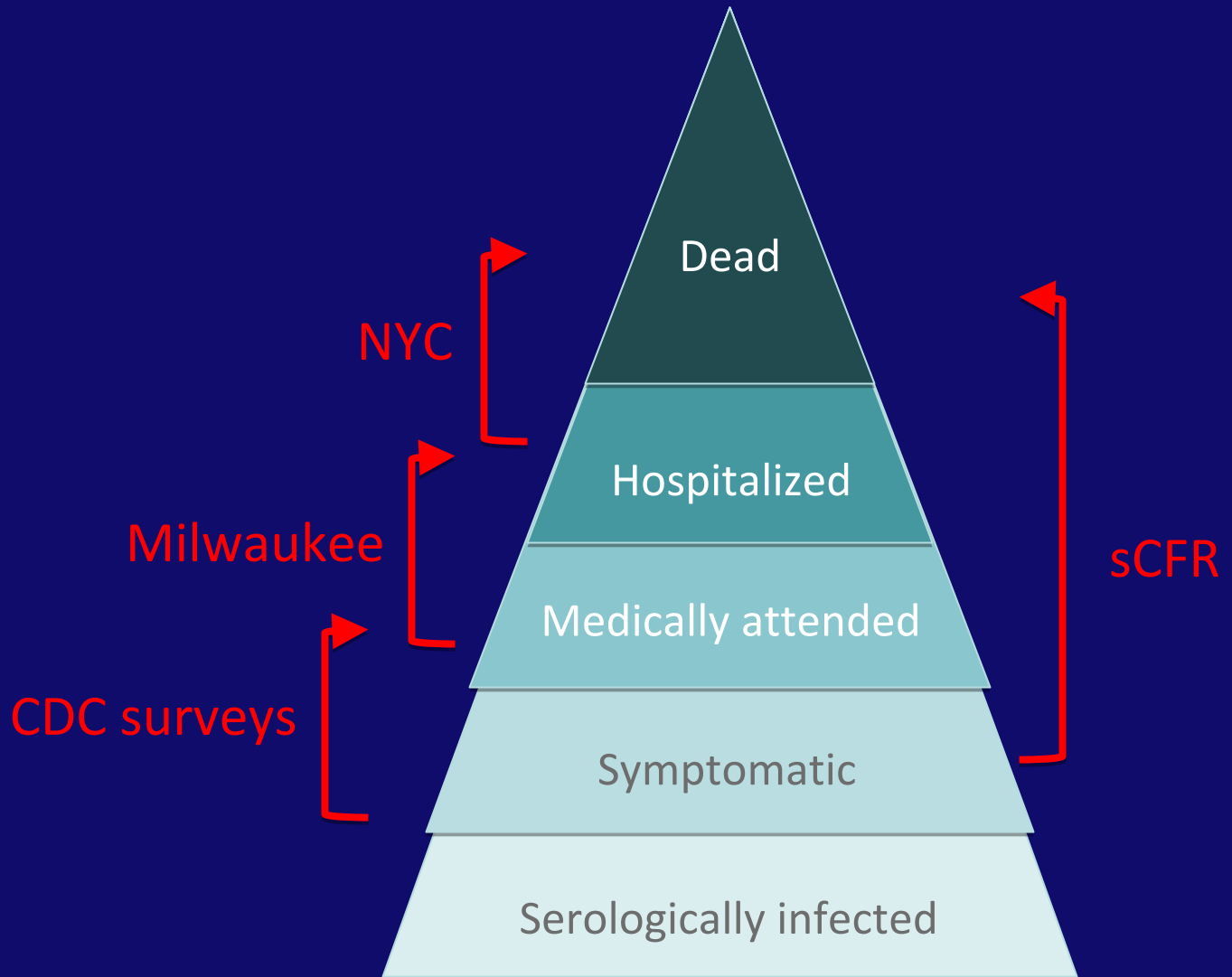
THE EMERGING INFLUENZA PANDEMIC: ESTIMATING THE CASE FATALITY RATIO

N Wilson (nick.wilson@otago.ac.nz)[1], M G Baker[1]
1. Department of Public Health, University of Otago, Wellington, New Zealand

the plausible range of the CFR for symptomatic infection by this pandemic strain in developed countries. All of the methods produce substantially lower values (range 0.06% to 0.0004%) than a previously published estimate for Mexico (0.4%). As these

- Garske et al. *BMJ* 14 Jul
  - CFR 0.2-1.2%
  - Focus on censoring bias

The Severity Pyramid



Age-specific Severity Estimates

	sCHR: ratio of hospitalizations to symptomatic cases	sCIR: ratio of ICU admissions to symptomatic cases	sCFR: ratio of deaths to symptomatic cases
0-4 yr	0.33% (0.21-0.63)	0.044% (0.026-0.078)	0.004% (0.001-0.011)
5-17 yr	0.11% (0.08-0.18)	0.019% (0.013-0.027)	0.002% (0.000-0.004)
18-64 yr	0.15% (0.11-0.25)	0.029% (0.021-0.040)	0.010% (0.007-0.016)
65+ yr	0.16% (0.10-0.30)	0.030% (0.016-0.055)	0.010% (0.003-0.025)
TOTAL	**0.16% (0.12-0.26)**	**0.028% (0.022-0.035)**	**0.007% (0.005-0.009)**
0-4 yr	2.45% (1.10-5.56)	0.321% (0.133-0.776)	0.026% (0.006-0.092)
5-17 yr	0.61% (0.27-1.34)	0.106% (0.043-0.244)	0.010% (0.003-0.031)
18-64 yr	3.00% (1.35-5.92)	0.542% (0.230-1.090)	0.159% (0.066-0.333)
65+ yr	1.84% (0.21-25.38)	0.100% (0.035-4.711)	0.028% (0.008-1.471)
TOTAL	**1.44% (0.83-2.64)**	**0.222% (0.134-0.458)**	**0.048% (0.026-0.096)**

Self-reported ILI denominator (NYC data only)

Self-reported frequency of seeking care (NYC/Milw./ CDC data)

Factors Affecting Cost Effectiveness of Vaccine

Three factors substantially affect the cost effectiveness of influenza vaccines in high risk and general populations:

- Vaccine efficacy
- Cost of vaccination
- Medical care expenditures averted, including medical care expenditures in extended years of life.

- Not usually considered in CE of Childhood Vaccines:
  - Impact on Education
  - Impact on Productivity and Labor Markets
  - Impact on Fertility
  - Impact on Savings
  - Impact on Foreign Direct Investments

COST-BENEFIT OF VACCINES IN US

- SMALLPOX — *$32 million every 20 days*
- MMR (Measles, Mumps & Rubella) — *$21 for every dollar spent on vaccine*
- DPT (Diphtheria, Pertussis, Tetanus) — *$29 for every dollar spent on vaccine*
- POLIO ERADICATION — *$3 billion annually*

Costs of Seasonal Influenza

- **In the US** the annual direct medical costs (hospitalization, doctors' office visits, medications, etc.) of influenza are estimated at up to $4.6 billion.
- Each year, up to 111 million workdays are lost because of influenza , costing American businesses more than $7 billion a year in sick days and lost productivity.
- Total direct and indirect costs (work days lost, school days lost, etc.) of a severe influenza epidemic are at least $12 billion.
- Conclusion: Despite variability in estimates:
  - Very cost-effective for high risk children
  - Variable cost-effectiveness or cost-benefit for low risk populations, dependent on vaccine cost and % high risk kids

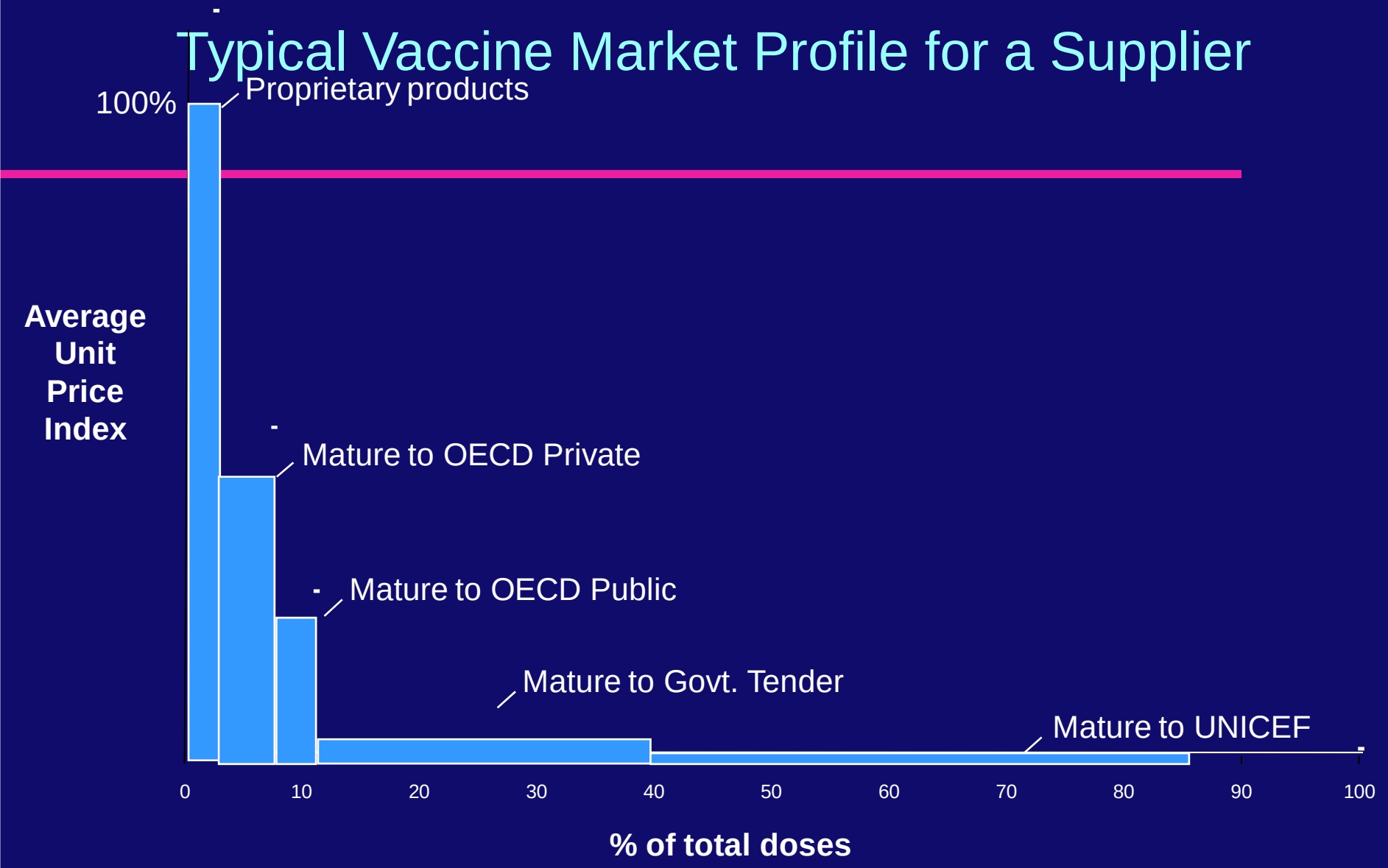
Meltzer et al, 2005

Cost Benefit Analysis in Malaysia

- The anti-influenza vaccination strategy reduced the absence of people from work by 77% and decreased the loss of working days by 82%. The ratio between the benefits of the vaccination strategy (less working days lost) and its costs was 12.12. The ratio remains favorable when the mean cost of a working day for the enrolled employees is used, resulting in a benefit-cost ratio of 9.45.

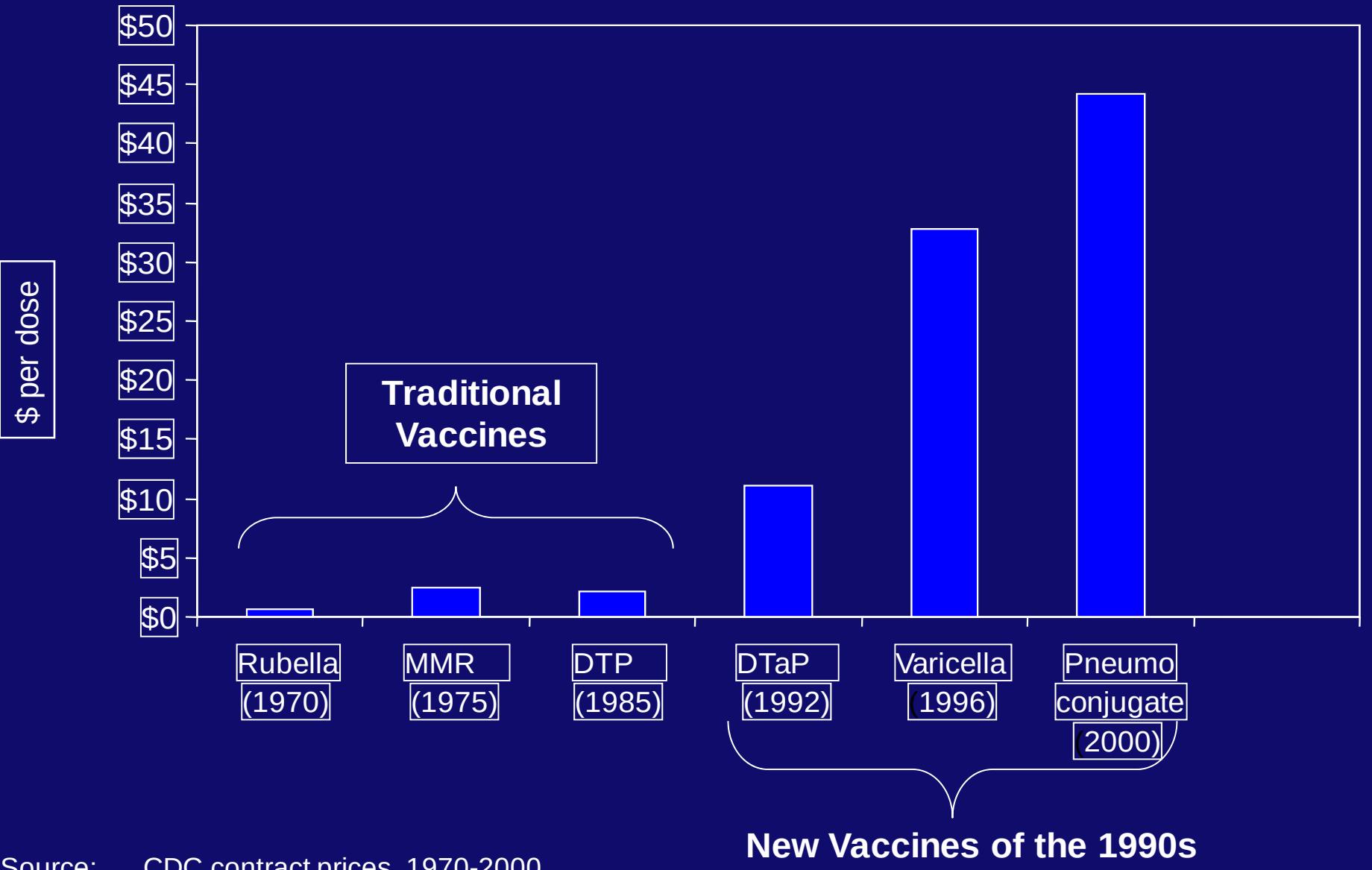
Snamprogetti (EMI Oil Co, Malasia)

Typical Vaccine Market Profile for a Supplier



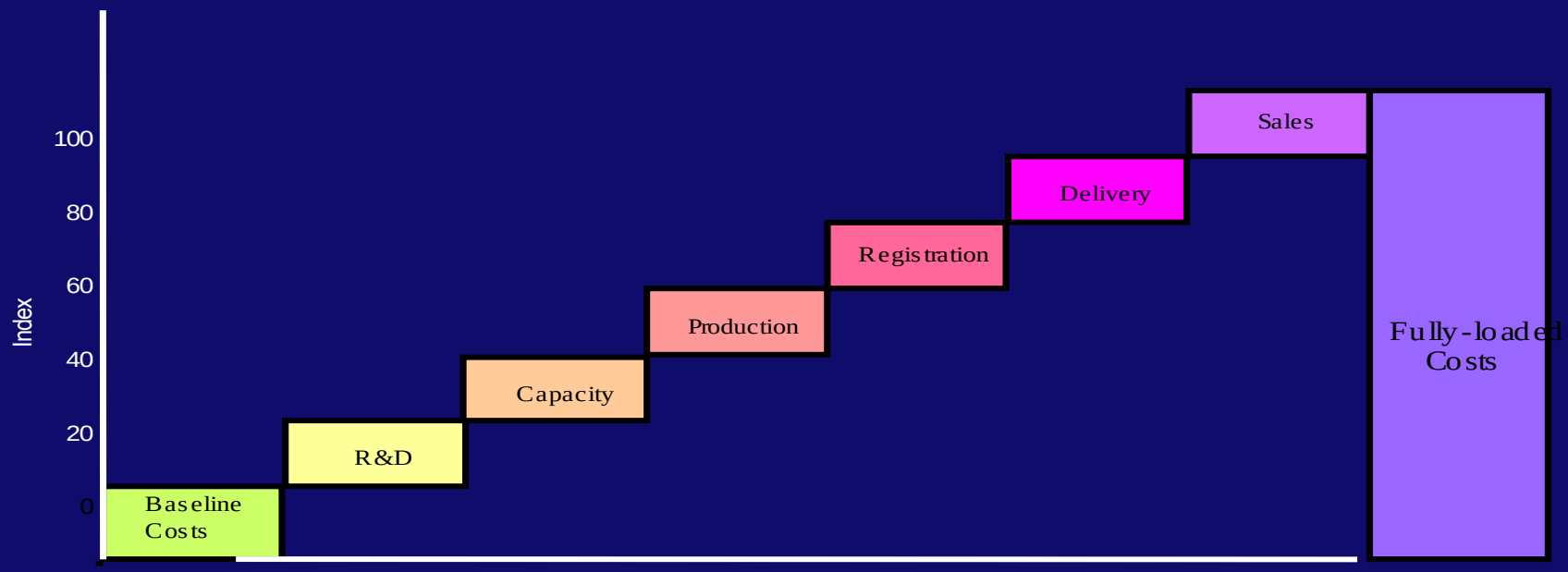
Source:UNICEF, Mercer analysis

Price of Traditional and New Vaccines



Source: CDC contract prices, 1970-2000

Risk at Each Stage of the Vaccine Life Cycle



- Clinical trials
- Factory production costs
- Licensing fees
- Production costs
- Quality Control

- Site problems
- Product promised after trial
- Parallel trials
- Different data hurts licensing

- Difficulty with
  - plans
  - facility
  - equipment
  - validation
  - staff

- Poor forecasting
  - Overruns
  - Underruns
- Raw materials failure/supply problems

- Uncertain regulatory pathway
- Complaints/ adverse event

- Slow uptake
- Can't reach target pop'n

- No funds to purchase
- Price Erosion

- All baseline costs
- Incremental opportunity costs/risk

Public Sector Assumes ALL Risk

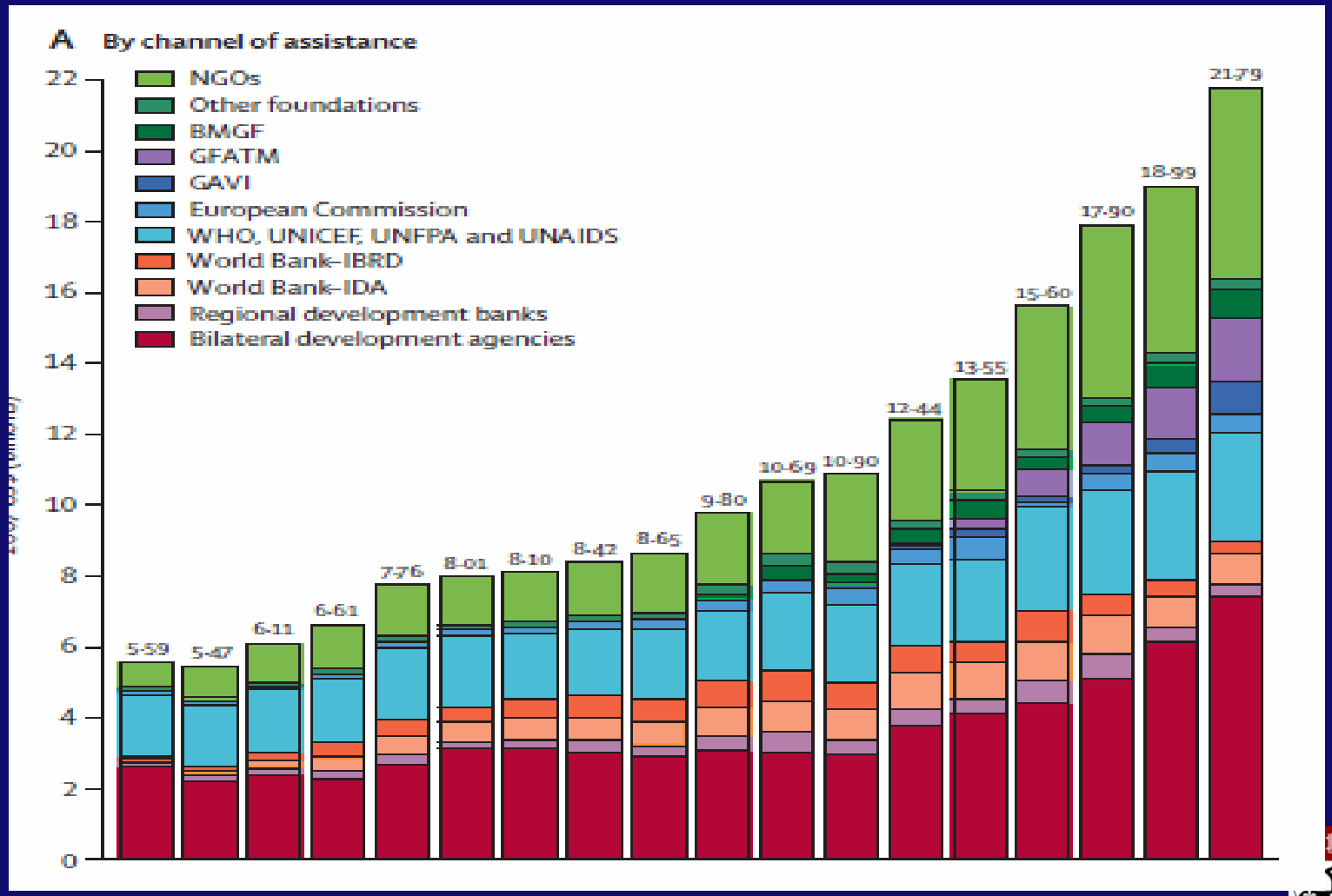
Private Sector Assumes ALL Risk

International Vaccine Institute

Created by UNDP to develop vaccines for infectious diseases of the poorest populations, e.g. cholera, typhoid, dengue

- Special Expertise in Effectiveness Trials
- Expertise and training in Vaccine Technology
- Training in Regulatory Processes for Developing Country Producers

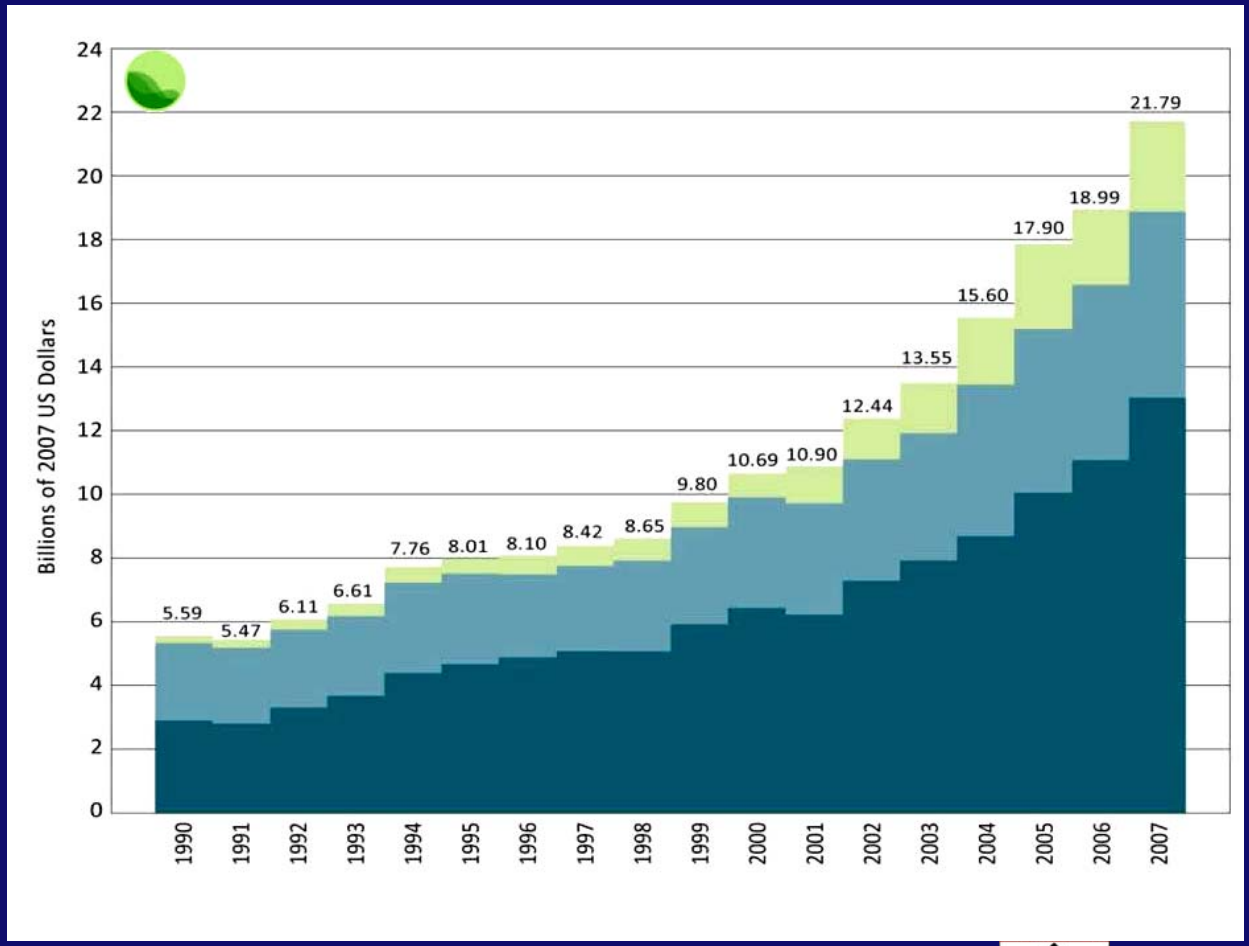
Increased Funding for Global Health
New Actors -1990-2007



Source: Ravishankar et al, 2009

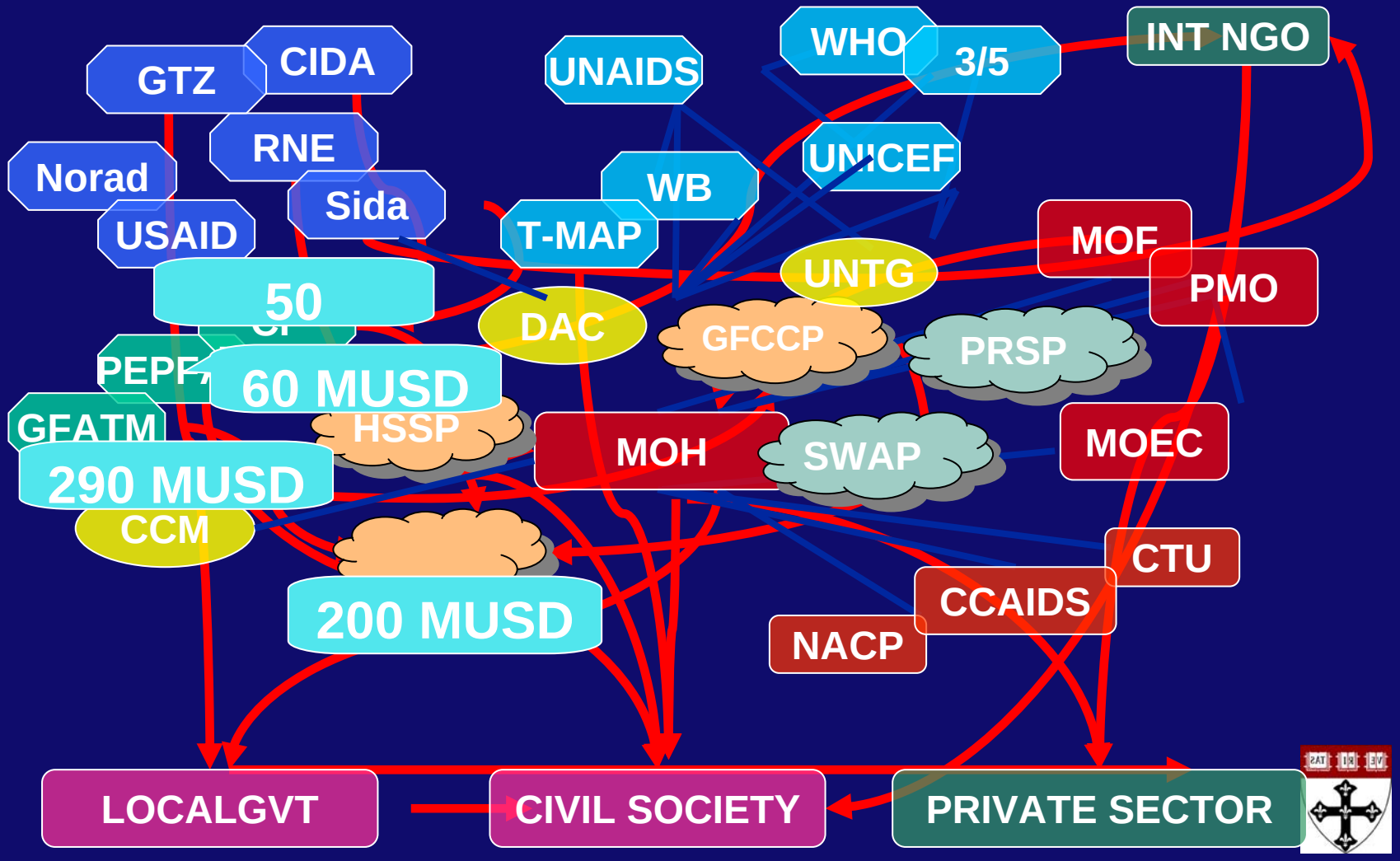
DAH composed of both monetary and in-kind transfers

DAH from 1990 to 2007 by type of assistance



Source: IHME DAH Database

Impact of Non-Harmonized Action & Insufficient Collaboration



Innovative Financing for Health

- IFFIm
- AMCs
- AMFm
- UNITAID
- Voluntary Travel surcharges
- IBRD/IDA Buy-downs
- Results Based Financing
- Proposed Patent Pooling
- Proposed currency transfer tax (0.005%)
- Proposed MassiveGood campaign ($2 gifts)

Innovative Funding Mechanisms
IFFIm

- The International Finance Facility for Immunization
  - launched in 2006 at the initiative of the United Kingdom Government.
  - Also supported by France, Italy, Spain, Sweden, Norway and South Africa who have together pledged to contribute US$ 5.3 billion to IFFIm over 20 years.
  - IFFIm to has a triple-A rating from the three major rating agencies.
-
- IFFIm raises finance by issuing bonds in the capital markets and so converts the long-term government pledges into immediately available cash resources. The long-term government pledges will be used to repay the IFFIm bonds.
- The World Bank acts as financial adviser and treasury manager
- No employees – Governed by 6 member Board

Advanced Market Commitments

AMCs

Innovative Financing for Health

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EMERGING INFECTIONS: SARS AND FLU

SARS

- Total Cases – 8422
  - China - 5327
  - Hong Kong - 1755
- Total Deaths- 1725
- Transmissibility $R_0 = 3$

1918 Influenza

- Total Deaths 20-40m
- Transmissibility $R_0 = 1.8 - 3$

Mills, C., Robins, J and Lipsitch, M. Nature 2004

EMERGING INFECTIONS: SARS AND FLU

SARS

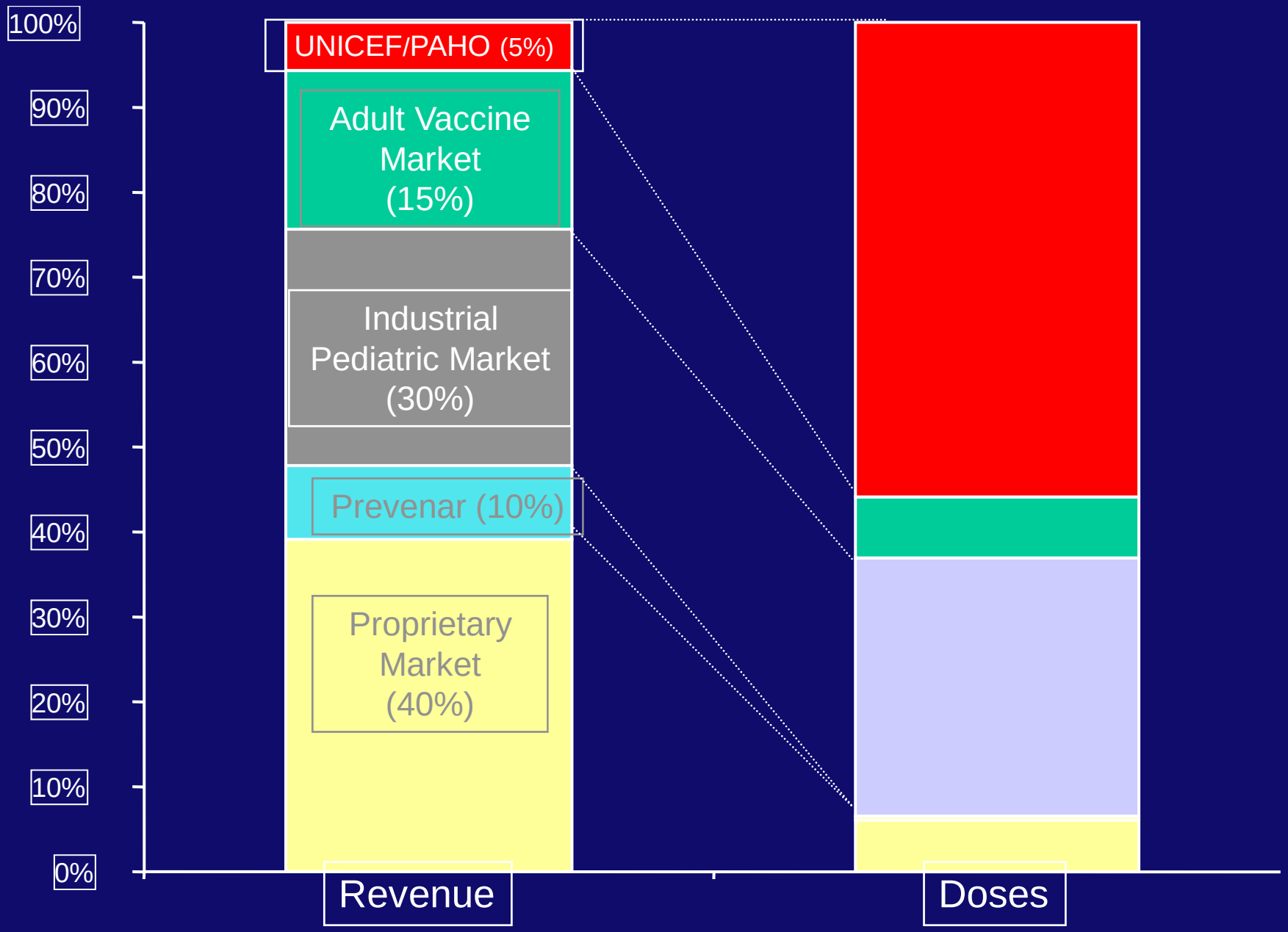
- Total Cases – 8422
  - China - 5327
  - Hong Kong - 1755
- Total Deaths- 1725
- Transmissibility $R_0 = 3$
- Serial Interval – 8.4d

1918 Influenza

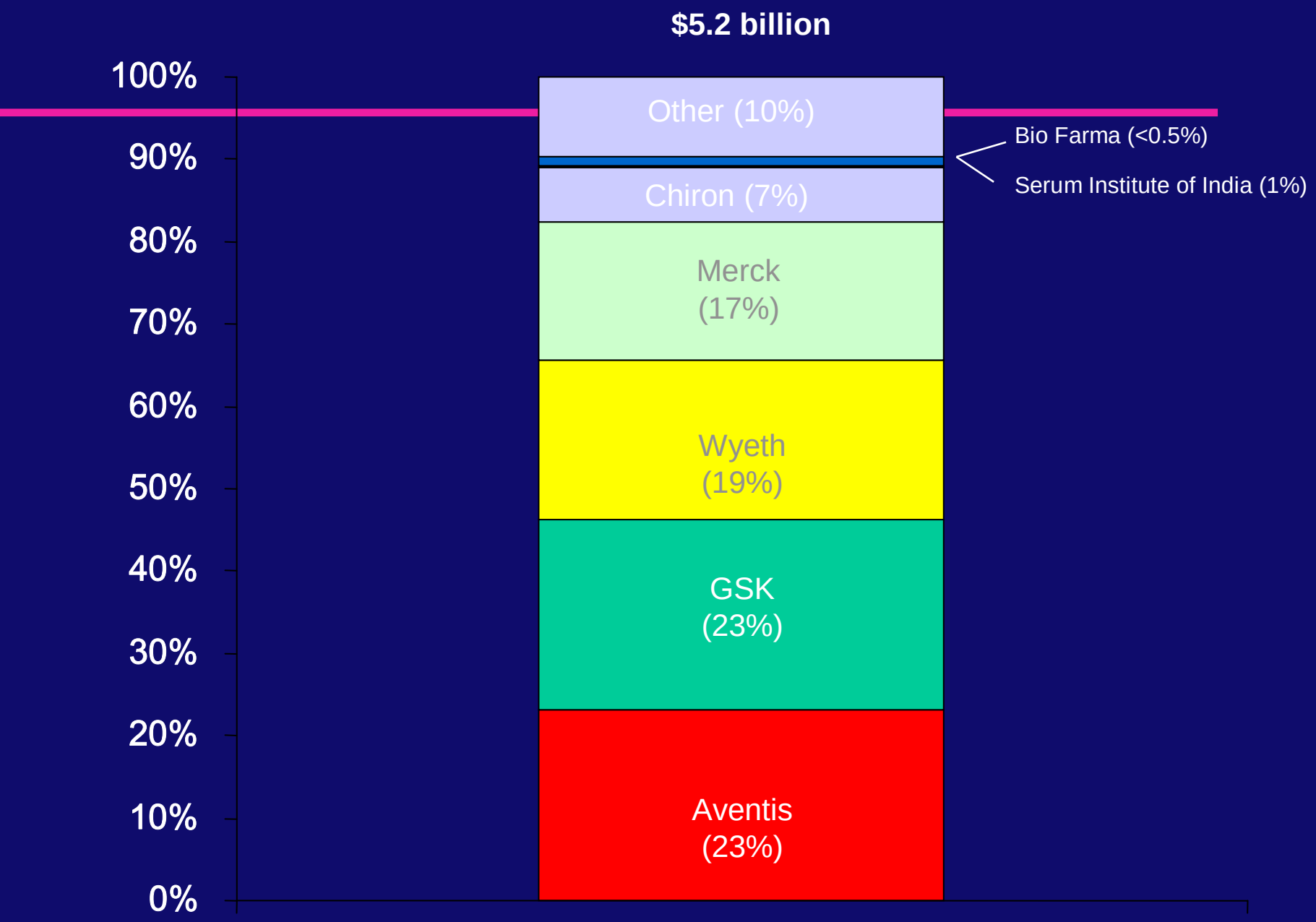
- Total Deaths 20-40m
- Transmissibility $R_0 = 1.8 - 3$
- Serial Interval – 4d (infectious at 2d)

Mills, C., Robins, J and Lipsitch, M. Nature 2004

INTERNATIONAL VACCINE MARKET BY REVENUE AND VOLUME



THE VACCINE PLAYERS IN VACCINE MARKET



Commodities and technical assistance accounted for 40% of DAH

- In-kind contributions in the form of technical assistance and drug donations constituted a significant share of total health aid ($8.7 out of $21.8 billion in 2007)

- Given current methods used to assign value to in-kind contributions, figures may be inflated

PLETHORA OF ACTORS IN ODA FOR HEALTH

Bi-lateral donors	Multi-lateral donors	Global Funds	NGOs	Private philanthropy	Private commercial sector
23 DAC donors	Worl	Global Fund,	International	Foundations such	Firms (e.g. Foreig
Bilateral	IMF	Global	National	Household	Commercial
Other	UN	Fast track	National		Private
Emergin	Regional	UN speci	UNIT		
	Others				

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